

AMENDMENTS TO THE SPECIFICATION

Please amend paragraphs on pages 9-14 encompassing “**brief description of the drawings**” of the originally filed specification as follows:

Brief Description of the Drawings

~~Fig. 1 is a picture showing~~ FIG. 1A-G show the morphology of MOMCs of the present invention. ~~[[a, b]]~~ (FIG. 1A, FIG. 1B) PBMCs were cultured on fibronectin in low-glucose DMEM supplemented with 10% FBS for 7 days, and observed with a phase contrast microscope. The original magnifications are $\times 80$ for ~~[[a]]~~ FIG. 1A, and $\times 40$ for ~~[[b]]~~ FIG. 1B. MOMCs were moved on a new fibronectin-coated plate and cultured for 24 hours. ~~[[c]]~~ FIG. 1C shows ~~A picture showing~~ the observation results with a phase contrast microscope ($\times 40$). ~~[[d, e]]~~ FIGS. 1D-E show ~~Pictures showing~~ observation results with an electron microscope ~~(d and e, $\times 5000$; f and g, $\times 30000$)~~ (FIG. 1D and FIG. 1E, $\times 5000$; FIG. 1F and FIG. 1G, $\times 30000$). A bundle of intermediate filaments is shown by an arrow, and a structure similar to a rod-shaped microtubulated body is shown by an arrowhead. L is for labyrinth-like endocytic vesicle; LD is for lipid droplet; N is for nucleus, and PS is for pseudopodia.

~~Fig. 2 is a figure showing~~ FIG. 2 shows the result of flow cytometric analysis of MOMCs of the present invention. PMBCs were cultured on fibronectin-coated plates and the adherent cells were harvested on Day 7. The cells were stained with a series of mAbs shown in the picture and analyzed by flow cytometry. The expression of the molecule of interest is shown as shaded histograms. Open histograms represent controls stained with isotype-matched control mAbs. The results shown are representative of at least three experiments.

~~Fig. 3 is a picture explaining~~ FIG. 3A-D demonstrate that MOMCs of the present invention originate from circulating CD14⁺ monocytes. ~~[[a)] (FIG. 3A)~~ PBMCs were cultured on fibronectin for 1 hour, and 1, 3, 5, 7, 10, and 14 days. The adherent cells were harvested and stained with FITC-conjugated anti-CD14 and PC5-conjugated anti-CD34 mAbs and analyzed by flow cytometry. The results shown are representative of three independent experiments. ~~[[b)] (FIG. 3B)~~ PBMCs depleted of CD14⁺ cells, CD34⁺ cells or CD 105⁺ cells, and mock-treated PMBCs were cultured on fibronectin for 7 days. The number of attaching cells per cm³ was counted, and the results are expressed as the ratio to the number of attached cells in the untreated PBMC culture. The results shown are the mean and SD from three donors. The asterisk in the figure indicates a significant difference compared with mock-treated PBMC cultures. ~~[[c)] (FIG. 3C)~~ MACS (Magnetic Cell Sorting)-sorted CD14⁺ monocytes were stained with PKH67 and cultured with or without unlabeled CD14⁻ cells (ratio 1:4) on fibronectin-coated or uncoated plastic plates for 7 days. The adherent cells were harvested, stained with PC5-conjugated anti-CD34 mAb, and analyzed by flow cytometry. The results shown are representative of three experiments. ~~[[d)] (FIG. 3D)~~ MACS-sorted CD14⁺ monocytes were stained with CFSE and cultured on fibronectin for 0, 1, 3, and 5 days. The adherent cells were harvested and stained with PC5-conjugated anti-CD14 mAb. The cells were analyzed by flow cytometry. The results shown are representative of three experiments.

~~Fig. 4 is a picture showing~~ FIG. 4A-D show the result of immunohistochemical analysis of MOMCs of the present invention. MOMCs generated by culturing PBMCs on fibronectin-coated plates for 7 days were moved onto fibronectin-coated chamber slides (The slides coated with type I collagen were only used for fibronectin staining). After 24 hours of culture, the above-mentioned slides were fixed with 10% formalin and stained with mAbs as indicated in the picture. The nuclei were counterstained

with hematoxylin. Original magnification is $\times 100$. The results shown are representative of at least three independent experiments.

~~Fig. 5 is a figure showing~~ FIGS. 5A-C show how the MOMCs of the present invention proliferate. MOMCs generated by culturing PBMCs on fibronectin-coated plates for 7 days were moved on fibronectin-coated chamber slides. MOMCs were further cultured for 1, 3, 5, 7, and 10 days, and stained with BrdU. The nuclei were counterstained with hematoxylin. [(a)] (FIG. 5A) A representative figure at Day 1 and Day 5. The arrow indicates nuclei positive for BrdU staining. [(b)] (FIG. 5B) At least 200 cells were counted to see the BrdU staining experiment result and the number of BrdU+ cells was calculated for individual slides cultured for 1, 3, 5, 7, and 10 days. The results shown are the mean and SD of five independent experiments. [(c)] (FIG. 5C) MOMCs were labeled with CFSE and were cultured on new fibronectin-coated plates for 0, 1, 3, 5 days. The adherent cells were collected and analyzed by flow cytometry. The results shown are representative of three independent experiments.

~~Fig. 6 is a picture showing~~ FIGS. 6A-K show osteogenic, myogenic, chondrogenic, and adipogenic differentiation of MOMCs of the present invention. MOMCs before and after three weeks of osteogenic induction were stained with Alizarin red [(a)] (FIG. 6A; magnification $\times 100$) or with alkaline phosphatase [(b)] (FIG. 6B; $\times 100$). The intracellular calcium deposition was measured in MOMCs and fibroblasts before and after osteogenic induction and expressed as microgram per microgram protein content [(c)] (FIG. 6C). Expression of mRNAs for osterix, bone sialoprotein II (BSP II), osteocalcin, CD34, CD45, CD14 and GAPDH were examined in MOMCs before and after 3 weeks of osteogenic induction and in osteosarcoma cell line [(d)] (FIG. 6D). MOMCs before and after 3 weeks of myogenic induction were stained, and SkM-actin staining [(e; $\times 200$)] (FIG. 6E; $\times 200$) or SkM-MHC staining [(f; $\times 200$)] (FIG. 6F; $\times 200$) were examined. Expression of mRNAs for

myogenin, SkM-MHC, CD34, CD45, CD14, and GAPDH was examined in MOMCs before and after 3 weeks of myogenic induction and in myoblast, muscle tissue, and in rhabdomyosarcoma cell line [(g)] (FIG. 6G). MOMCs before and after 3 weeks of chondrogenic induction were stained and type II collagen staining were examined [(h; ×40)] (FIG. 6H; ×40). Expression of mRNAs for $\alpha 1$ (type II) and $\alpha 1$ (type X) collagen, CD34, CD45, CD14, and GAPDH was examined in MOMCs before and after 3 weeks of chondrogenic induction and in a chondrosarcoma cell line [(i)] (FIG. 6I). MOMCs before and after 3 weeks of adipogenic induction were stained with Oil-red-O [(j; ×200)] (FIG. 6J; ×200). Expression of the mRNAs for PPAR γ , aP2, CD34, Cd45, CD14 and GAPDH was examined in MOMCs before and after three weeks of adipogenic induction and in fat tissue [(k)] (FIG. 6K). The results shown are representative of at least five experiments.

~~Fig. 7 is a picture showing~~ FIGS. 7A-H show the coexpression of CD45 (green) and tissue-specific transcription factors (red) in MOMCs of the present invention that underwent 1 week of mesenchymal differentiation. MOMCs before induction treatment [(a-d)] (FIGS. 7A-D) and MOMCs treated for osteogenic [(e)] FIG. 7E, myogenic [(f)] FIG. 7F, chondrogenic [(g)] FIG. 7G or adipogenic [(h)] FIG. 7H induction for 1 week were examined for the immunohistochemical localization of CD45 in combination with Cbfa1/Runx2 [(a and e)] (FIG. 7A and FIG. 7E), MyoD [(b and F)] (FIG. 7B and FIG. 7F), Sox-9 [(c and g)] (FIG. 7C and FIG. 7G), or PPAR γ [(d and h)] (FIG. 7D and FIG. 7H). The cells were observed with confocal laser fluorescence microscopy (original magnification ×200). The results shown are representative of three experiments.

~~Fig. 8 is a picture showing~~ FIGS. 8A-D show how MOMCs of the present invention differentiate into myocardium. Nestins (brown) expressed in MOMCs cocultured with Wistar rat-cultured myocardial cells for 8 days were immunostained [(A;)]

(FIG. 8A ×200). After labeling cell membrane with fluorescent PKH67 (green), MOMCs were cocultured with Wistar rat-cultured myocardial cells for 7 days, and were double fluorescently immunostained with Nkx 2.5 (red), a myocardial cell-specific transcription factor, and CD45 (blue), a hematopoietic marker [(B;)] (FIG. 8B ×200). After labeling cell membrane with fluorescent PKH67 (green), MOMCs were cocultured with Wistar rat-cultured myocardial cells for 8 days, and were double fluorescently immunostained with eHAND (red), a myocardial cell-specific transcription factor, and CD45 (blue), a hematopoietic marker [(C;)] (FIG. 8C ×200). MOMCs were cocultured with Wistar rat-cultured myocardial cells for 3, 6, 9, 12 days and expression of the mRNAs for myosin light chain (MLC2v), a myocardial cell-structural protein [(D;)] (FIG. 8D). The results shown are representative of three experiments.

~~Fig. 9 is a picture of~~ FIGS. 9A-E show how MOMCs of the present invention differentiate into neurons. Nestins (brown), which are markers expressing in nerve/myocardial progenitors, and being expressed in MOMCs cocultured with Wistar rat-cultured neurons for 8 days were immunostained [(A;)] (FIG. 9A ×200). After labeling cell membrane with fluorescent PKH67 (green), MOMCs were cocultured with Wistar rat-cultured neurons for 4 days, and were double fluorescently immunostained with NeuroD (red), a neuron-specific transcription factor, and CD45 (blue), a hematopoietic marker [(B;)] (FIG. 9B ×200). MOMCs were cocultured with Wistar rat-cultured neurons for 3 days, and were double fluorescently immunostained with nestin (brown) and Neurogenin 2 (red), a neuron-specific transcription factor [(C;)] (FIG. 9C ×200). PKH67-labeled MOMCs (green) were cocultured with Wistar rat-cultured neuron for 3 days, and were double fluorescently immunostained with Hu (red), a mature-nerve marker [(D;)] (FIG. 9D ×200). PKH67-labeled MOMCs were cocultured with Wistar rat-cultured neuron for 9 days, and were

fluorescently immunostained with NeuN (red), a mature-nerve marker FIG. 9E (×200).

The results shown are representative of three experiments.

~~Fig. 10 is a picture showing~~ FIGS. 10A-C show how MOMCs of the present invention differentiate into endothelial cells. MOMCs induced to differentiate in a EBM-2 medium, a maintenance medium of endothelial cells, for 7 days, changed to a morphology having multiple projections from a spindle shape FIG. 10A (×200). CD34 and endothelial cell-specific vWF, eNOS, VEGFR2/KDR/Flk-1, expressed in MOMCs induced to differentiate in an EBM-2 medium for 7 days, were immunostained (brown) FIG. 10B (×200). Expression of the mRNAs for Flt-1, VEGFR2/KDR/Flk-1, CD31, CD144, vWF, CD34, CD45, CD14, and GAPDH, expressed in endothelial cells after 7-day culture of MOMCs in an EBM-2 medium, was examined FIG. 10C. The results shown are representative of three experiments.